Polyoxygenated Cyclohexenes and Other Constituents of Cleistochlamys kirkii Leaves

Nyandoro, Stephen S.; Munissi, Joan J.E; Gruhonjic, Amra; Duffy, Sandra; Pan, FangFang; Puttreddy, Rakesh; Holleran, John P.; Fitzpatrick, Paul A.; Pelletier, Jerry; Avery, Vicky M.; Rissanen, Kari; Erdelyi, Mate

Abstract:

Thirteen new metabolites, including the polyoxygenated cyclohexene derivatives cleistodiendiol (1), cleistodienol B (3), cleistenechlorohydrins A (4) and B (5), cleistenediols A–F (6–11), cleistenonal (12), and the butenolide cleistanolate (13), 2,5-dihydroxybenzyl benzoate (cleistophenolide, 14), and eight known compounds (2, 15–21) were isolated from a MeOH extract of the leaves of Cleistochlamys kirkii. The purified metabolites were identified by NMR spectroscopic and mass spectrometric analyses, whereas the absolute configurations of compounds 1, 17, and 19 were established by single-crystal X-ray diffraction. The configuration of the exocyclic double bond of compound 2 was revised based on comparison of its NMR spectroscopic features and optical rotation to those of 1, for which the configuration was determined by X-ray diffraction. Observation of the co-occurrence of cyclohexenoids and heptenolides in C. kirkii is of biogenetic and chemotaxonomic significance. Some of the isolated compounds showed activity against Plasmodium falciparum (3D7, Dd2), with IC_{50} values of 0.2–40 μM, and against HEK293 mammalian cells (IC_{50} 2.7–3.6 μM). While the crude extract was inactive at 100 μg/mL against the MDA-MB-231 triple-negative breast cancer cell line, some of its isolated constituents demonstrated cytotoxic activity with IC_{50} values ranging from 0.03–8.2 μM. Compound 1 showed the most potent antiplasmodial (IC_{50} 0.2 μM) and cytotoxic (IC_{50} 0.03 μM, MDA-MB-231 cell line) activities. None of the compounds investigated exhibited translational inhibitory activity in vitro at 20 μM.